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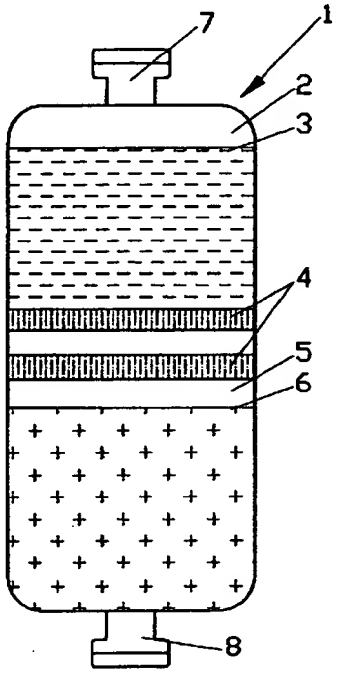
(54)【発明の名称】　医療用容器

(57)【要約】

【目的】　製造前、製造後、或いは長期保存後のどの段階であってもＰＨ値がほぼ一定に維持され、且つ炭酸ガス濃度も一定に維持される炭酸成分入り医療用溶液を収容した医療用容器を提供。

【構成】　一の室に重炭酸又は炭酸から成る炭酸成分溶液を液密に収容し、他の室に炭酸成分以外の電解質からなる母液を液密に収容した多室容器からなり、使用時に上記各室同士を連通して炭酸成分溶液と母液とを混合して炭酸成分入り医療用溶液が提供される医療用容器において、上記混合後の医療用溶液中に重炭酸イオン量が１０～３５ｍｍｏｌ／Ｌの範囲で含まれるように上記一の室に上記炭酸成分が収容され、上記混合後の医療用溶液中に上記炭酸成分の一部が炭酸（炭酸イオン及び炭酸ガス）を１０～８０ｍｍＨｇの範囲で生じるように上記他の室の母液に過剰酸が含まれていることを特徴とする。



【特許請求の範囲】
【請求項１】一の室に重炭酸又は炭酸から成る炭酸成分溶液を液密に収容し、他の室に炭酸成分以外の電解質からなる母液を液密に収容した多室容器からなり、使用時に上記各室同士を連通して炭酸成分溶液と母液とを混合して炭酸成分入り医療用溶液が提供される医療用容器において、
上記混合後の医療用溶液中に重炭酸イオン量が１０～３５ｍｍｏｌ／Ｌの範囲で含まれるように上記一の室に上記炭酸成分が収容され、
上記混合後の医療用溶液中に上記炭酸成分の一部が炭酸（炭酸イオン及び炭酸ガス）を１０～８０ｍｍＨｇの範囲で生じるように上記他の室の母液に過剰酸が含まれていることを特徴とする炭酸成分入り医療用容器。
【請求項２】上記炭酸成分溶液には保存時に炭酸成分の分解喪失を防止するための過剰アルカリ塩（Ｂ）を添加し、上記母液中に過剰酸を、０．５ｍＥｑ／Ｌ≦過剰酸（Ａ）-過剰アルカリ塩（Ｂ）≦５．０ｍＥｑ／Ｌの範囲となるように添加することを特徴とする請求項１記載の医療用容器。
【請求項３】少なくとも上記一の室をガスバリアー性の包装材で包装してなることを特徴とする請求項２記載の医療用容器。
【請求項４】上記包装材の包装が真空包装であることを特徴とする請求項３記載の医療用容器。

【発明の詳細な説明】
【０００１】
【産業上の利用分野】本発明は、輸液、透析液、臓器保存液等を収納した医療用容器に関するものであり、特に、安定性に欠ける炭酸成分を含有させた医療用溶液を収容した医療用容器に関するものである。
【０００２】
【従来の技術】一般に重炭酸ナトリウム溶液を樹脂容器等に収容すれば、加熱或いは保存中に分解し、炭酸ガスが発生し、炭酸ガスは容器壁を透過して消失する。かかる分解により溶液中には［ＯＨ⁻］が電離平衡のため増加し、溶液のＰＨ値は上昇する。このため、医療用容器を長く保存するために、医療用容器をガスバリアー性の包装体で密封包装し、包装体内に炭酸ガスを導入したり、炭酸ガス発生型の脱酸素剤を配して医療用容器の外側を炭酸ガス雰囲気とすることにより、樹脂容器内の炭酸ガスが樹脂容器外にでることを阻止した技術が提案されている（特許第２５２７５３２号公報、特開昭６-１０５９０５号公報）。
【０００３】
【発明が解決しようとする課題】しかしながら、従来の炭酸成分を含有した医療用容器の製造方法には以下の点で問題が見られる。包装体に炭酸ガスを収容したものも、或いは脱酸素剤を配したものも、医療用容器内の溶液の初期ＰＨ値は蒸気滅菌処理時の若干の炭酸イオンの喪失のため８．３２或いは８．６０と高い。そして、１０日後以降に医療用容器内のＰＨ値が８．０以下を示す。これは、医療用容器内の溶液が容器壁を透過してくる炭酸ガスを取り込んだものと考えられる。しかし、このような医療用容器にあっては、初期組成から明らかに相違し、どの程度の炭酸ガスが医療用容器内の溶液に溶け込んだか不明である。また、炭酸ガスを過剰に取り込んだ溶液では溶液中のカルシウムイオンやマグネシウムイオンと反応して沈殿物を生じるおそれがある。従って、本発明は製造前、製造後、或いは長期保存後のどの段階であってもＰＨ値がほぼ一定に維持され、且つ炭酸ガス濃度も一定に維持される炭酸成分入り医療用溶液を収容した医療用容器を提供することにある。
【０００４】
【課題を解決するための手段】本発明は、一の室に重炭酸又は炭酸から成る炭酸成分溶液を液密に収容し、他の室に炭酸成分以外の電解質からなる母液を液密に収容した多室容器からなり、使用時に上記各室同士を連通して炭酸成分溶液と母液とを混合して炭酸成分入り医療用溶液が提供される医療用容器において、上記混合後の医療用溶液中に重炭酸イオン量が１０～３５ｍｍｏｌ／Ｌの範囲で含まれるように上記一の室に上記炭酸成分が収容され、上記混合後の医療用溶液中に上記炭酸成分の一部が炭酸（炭酸イオン及び炭酸ガス）を１０～８０ｍｍＨｇの範囲で生じるように上記他の室の母液に過剰酸が含まれていることを特徴とする炭酸成分入り医療用容器を提供することにより、上記目的を達成したものである。
【０００５】上記医療用容器は通常可撓性壁を有する樹脂容器である。可撓性壁は撓むことにより容器内の容積が容易に変化するものであれば良い。また容器壁は内容物の確認できる程度に透明性を有することが望ましい。容器内での薬剤の状態を確認する上で必要となるからである。上記容器は、インフレーションフィルム、チューブ、シート及びフィルムから成形したもの、押出成形、射出成形、又はブロー成形したものである。樹脂容器の樹脂素材としてはポリオレフィン系樹脂、塩化ビニル、塩化ビニリデン系樹脂、ポリエステル系樹脂、ポリビニルアルコール系樹脂、ポリアクリルニトリル系樹脂、ポリアクリル酸系樹脂、ポリアミド系樹脂等の汎用樹脂である。また樹脂容器は単層又は多層で形成されていても良い。樹脂容器内の薬剤と接触する最内層は、薬剤に影響を与えない、また溶出物が生じない樹脂層であることが望ましい。このような樹脂としては、ポリオレフィン系樹脂が望ましく、例えば、低、中、高-密度ポリエチレン、ポリプロピレン等の低級オレフィン樹脂等が挙げられる。また、樹脂容器壁にはガスバリアー性層が形成されていることが望ましい。特に、酸素等を容易に透過しない層であることが望ましい。このようなガスバリアー性層としては、殆ど、又は全くガスを透過させないアルミニウム等の金属層や酸化珪素、酸化マグネシウム、

酸化チタン等の無機蒸着層であり、またポリ塩化ビニリデン、ポリエステル、ナイロン、エチレン-ビニルアルコール共重合体、フッ素系樹脂等のようにガスバリアー性の高い樹脂層である。ガスバリアー性層の酸素透過量は４０ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ（温度：２０℃）以下、特に、３０ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ以下、また好ましくは５ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ以下、更には１ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ以下であることが望ましい。また、樹脂容器の壁は内部の薬剤が確認できる程度に透明性を有することが望まれる。このため、ガスを全く透過させない優れた機能を有する上記アルミニウム層等の金属層から成る壁は少なくとも一部においてその金属層が剥離可能に形成されていることが望ましい。かかる層を有した樹脂容器においては高圧蒸気滅菌時に内部の薬剤の熱による変質を十分に防止することができる。

【０００６】上記炭酸成分と母液とを分けて液密充填し蒸気滅菌処理する。炭酸成分溶液と母液とを分けて液密に収容するとは、上記炭酸成分溶液と上記母液を個別に収容する複数の室を有した樹脂製の容器を用いても良い。このような容器が複数の室に分割される場合には室と室とを隔離する部分に容器壁越しの操作により室と室とを互いに連通する連通手段を構成することが望ましい。かかる連通手段とは、閉鎖型管の端部を容器壁越しに破断して該管を連通管とするもの、隔離部分を挟持クリップ等で止めたもの、或いは、隔離する部分を外側からの操作により剥離可能なピールシール部とするもの等、その他公知の無菌的連通が可能な手段である。また、上記炭酸成分と上記母液とを別個の容器に収容してこれを接続した複数容器からなるものでも良い。容器同士の接続には上記ピールシール部で構成した容器端部同士を接続して使用時に容器越しの操作で連通可能な構造となるもの、容器同士をそれ自体公知の連通針を備えた連通手段で連通操作可能なもの等が挙げられる。尚、容器が複数容器から構成されるものは、少なくとも一方はガラス製の容器であっても良いが、好ましく樹脂製容器同士から構成することが望ましい。また特に、複数の室は容器越し及び包装体越しに連通過能なピールシール部で形成或いは接続されている容器であることが望ましい。

【０００７】即ち、上記ピールシール部は弱シール部とも称され、外部から室或いは容器を圧迫し、内部が一定の昇圧状態になったときに剥離する隔離シール部である。上記ピールシール部の剥離強度は、室内の圧が０．０１～１．０Ｋｇｆ／cm^2、特に、０．０５～０．５Ｋｇｆ／cm^2の昇圧で剥離する強度が望ましい。上記範囲を下回る強度であれば、製造、運搬、保存時等の隔離状態を保つための安全性に欠ける。上記範囲を上回る強度であれば、用時に室と室同士の連通操作を容易にすることができなくなるおそれがある。樹脂容器の内層同士のピールシールの形成或いは完全固着シールを形成する場合にはそれ自体公知の技術を用いることができ、これらのシールを確実に異ならせて形成するためには、樹脂容器の内層が異なる樹脂のブレンド物であることが望ましい。特に、異なる樹脂は、熱溶融開始温度、或いはピカッド軟化点が異なり、相溶性のあまりない樹脂ブレンド物からなることが望ましい。かかるブレンド物層を有することより、同一の内層で、完全な密封シール接着のシール温度条件設定が簡単にできる一方、ピールシール接着のシール温度条件設定も簡単にできる。また、ピールシール接着に求められるシール強度、即ち、使用時の外力による易剥離性と、保存時に剥離が生じないシール強度との関係を厳密に設定することができる。即ち、内層に相溶性の異なる樹脂を溶融混合し、これをシート状に成形することによって、ミクロ的に熱接着性の異なる部分に分離した表面としたものである。そして、任意の温度におけるそのシートの表面相互のミクロ的な部分の熱溶融性を決めることにより、シール強度の強弱を正確に付け、上記効果を容易に達成するものである。

【０００８】上記母液は輸液、透析液、臓器保存液に用いられる成分であり、例えば、ナトリウム、カリウム、マグネシウム、カルシウム、クロール、リン等、その他の人体に存在する無機電解質、酢酸、乳酸、クエン酸等、その他の人体に存在する有機電解質等であり、また、電解質の他に糖類、アミノ酸、蛋白質、脂肪等のエネルギー、必要により生理活性物質、ビタミン等も含まれる。尚、母液は樹脂容器に無菌的に充填しても良いが、樹脂容器の収容室に液密収容した後、蒸気滅菌処理されたものである。かかる滅菌処理により、母液の滅菌が確実になされ、患者への安全な投与ができるからである。上記一の室の炭酸成分溶液は、上記混合後の医療用溶液中に重炭酸イオン量が１０～３５ｍｍｏｌ／Ｌの範囲、特に１５～３０ｍｍｏｌ／Ｌ、より好ましくは２０～２８ｍｍｏｌ／Ｌの範囲になるように重炭酸塩或いは炭酸塩を溶解したものである。血漿中の重炭酸イオン濃度は２２～２６ｍＥｑ／Ｌが正常とされ、医療用溶液中にはかかる正常値の範囲で含ませることが望ましいが、輸液剤等は一時的に投与されるものであるため、正常値より投与値は広い範囲で許容できる。また炭酸成分溶液中にはナトリウム、カリウム等のアルカリ塩が上記炭酸成分である重炭酸イオン量と同等又はそれ以上を含有させることが望ましい。アルカリ塩が同等又はそれ以上含まれる場合には炭酸が弱酸であることから上記一の室内がアルカリ性に維持され、炭酸成分が炭酸ガスとして容器外に喪失することを極力抑えることができる。上記炭酸成分溶液の容積容量は母液容積容量の１／１０～１／１であることが望ましい。上記炭酸成分溶液の容積容量が上記範囲を下回ると充填誤差が大きくなり製造ラインに支障を来す。

【０００９】上記混合後の医療用溶液中に上記炭酸成分

の一部から１０～８０ｍｍＨｇの範囲で炭酸（炭酸イオン及び炭酸ガス）が生じるように上記他の室の母液には過剰酸が含まれる。母液は電解質溶液であるため通常、溶液中には｛OH^-、X^-、Y^-、Z^-、・・・｝と｛H^+、A^+、B^+、C^+・・｝との種々の陽及び負イオンが解離して存在している。そして、ＰＨ値が７付近であれば、水素イオン及び水酸基イオンを除いた場合でも｛X^-、Y^-、Z^-・・｝と｛A^+、B^+、C^+・・｝との陽・負電解質イオン量は等しい。しかし、負電解質を陽電解質より過剰に存在させた場合、過剰負電解質イオン量≒｛X^-、Y^-、Z^-・・｝－｛A^+、B^+、C^+・・｝となり、かかる負電解質イオン量と溶液中の水素イオン［H^+］とが平衡を保ちＰＨ値が下がる。これが過剰酸状態である。このような過剰酸が存在する母液にあっては、例えば２５．０ｍｍｏｌ／Ｌに相当する重炭酸ナトリウムからなる炭酸成分を過剰酸１．０ｍＥｑ／Ｌの母液に混合すると、炭酸ガス及び炭酸イオンが発生する。重炭酸は母液中の塩酸、乳酸、酢酸等よりも弱酸であるため、混合前まで重炭酸イオンと平衡関係にあったナトリウムイオンの２５ｍｍｏｌ／Ｌ中、混合後の医療用溶液中では過剰酸の１ｍＥｑ／Ｌ量だけ電離関係を持つ。ここで、その他の電解質の緩衝作用により混合医療用液のＰＨ値が７付近に維持されると、水酸基イオンも水素イオンもナノ単位量であるため、重炭酸イオンの２５ｍＥｑ／Ｌ中１ｍｍｏｌの［HCO_3^-］は［H^+］と結合して、炭酸ガスとして溶液中に解けるか、一部は溶液外に放出される。従って、混合医療用溶液中の重炭酸イオンは２４ｍＥｑ／Ｌとなり、医療用溶液中には炭酸ガスが発生して一部又は全部が溶解されて、炭酸ガスは下記式のヘンダーソン・ハッセルバルヒの式に従って溶液のＰＨ値に寄与する。ＰＨ値＝６．１＋Ｌｏｇ［HCO_3^-］／［０．０３×Ｐ（CO_2）］

【００１０】本発明に係る医療用容器では、混合医療用溶液中に炭酸ガスが１０～８０ｍｍＨｇの範囲で生じる。このため、理論上、過剰酸は８０×０．０３ｍＥｑ／Ｌ～１０×０．０３ｍＥｑ／Ｌ、即ち２．４～０．３ｍＥｑ／Ｌの範囲で含まれる。しかし、過剰酸に対して全て炭酸ガスが混合溶液中に溶解せずに外界にも放出される。かかる炭酸ガスの放出量は発生する炭酸量にもよるが、１００ｍｍＨｇ～２００ｍｍＨｇの間では約５０％が放出され、５０ｍｍＨｇ～９０ｍｍＨｇの間では約４０％程度が放出される。従って、かかる量を考慮すれば、過剰酸は０．５～５ｍＥｑ／Ｌで存在することができ、特に１．０～２．４ｍＥｑ／Ｌの範囲で存在することが望ましい。尚、本発明に係る混合医療用溶液中の炭酸濃度は上記ヘンダーソン・ハッセルバルヒの式から求めるものである。また過剰酸は炭酸を混合医療用溶液中に発生させる目的とする酸である。例えば、炭酸成分の一の室に重炭酸イオンと当モル量のナトリウム等の塩が含まれない場合、即ち、炭酸成分のアルカリ性を高めるため水酸化ナトリウム等を加えて重炭酸イオンより過剰アルカリ塩（Ｂ）が含まれる場合には、母液中の過剰酸は炭酸ガスの発生を目的とする量の他に、かかる過剰アルカリ塩と同等の酸、例えば塩酸等が更に加算されるものである。

【００１１】このように構成された本発明に係る炭酸成分入り医療用容器では、製造後において炭酸ガス等の吸収或いは補給をする必要がないため、医療用溶液に変動が生じない。また使用時に各室同士を連通するのみで炭酸ガスが医療用溶液中に生じ、体液とほぼ同様な成分組成を維持させることができる。特に、血漿中に近い重炭酸イオン量と炭酸ガスとを存在させ、ＰＨ値も血漿に近い値とすることができる。このため、従来から生じる乳酸アシドーシス等を起こすことがない。

【００１２】本発明に係る請求項２記載の医療用容器は、請求項１記載の医療用容器において、上記炭酸成分溶液には保存時に炭酸成分の分解喪失を防止するための過剰アルカリ塩（Ｂ）を添加し、上記母液中に過剰酸を、０．５ｍＥｑ／Ｌ≦過剰酸（Ａ）－過剰アルカリ塩（Ｂ）≦５．０ｍＥｑ／Ｌの範囲となるように添加することを特徴とする。上記一の室に収容される炭酸成分溶液に過剰アルカリ塩（Ｂ）を添加すると炭酸成分が分解して室外にでることが極力抑えられる。通常、医療用容器を高圧蒸気滅菌処理したときの加熱により炭酸成分が分解し易くなる。保存時に不用意に高温下に晒した場合にも炭酸成分の一部が炭酸ガスとして喪失するおそれが生じる。しかし、重炭酸イオン量よりアルカリ塩（Ｂ）を過剰にした炭酸成分溶液にあっては、炭酸成分の一部が炭酸ガスとして放出するのを防止する。

【００１３】本発明に係る請求項３記載の医療用容器は、請求項２記載の医療用容器において、少なくとも上記一の室をガスバリアー性の包装材で包装してなることを特徴とする。ガスバリアー性の包装材で医療用容器の全体を包装しても良く、また上記一の室のみを包装しても良い。上記一の室に過剰アルカリ塩（Ｂ）が存在すると、保存時に外界の炭酸ガスを容器越しに吸収するおそれがある。このため、炭酸成分量が保存中に変わり、医療用溶液の安定性に問題が生じる。しかし、上記ガスバリアー性の包装材で上記一の室を包装することにより外界から炭酸ガスを吸収することがない。本発明に係る請求項４記載の医療用容器は、請求項３記載の医療用容器において、上記包装材の包装が真空包装であることを特徴とする。保存時に不用意に高温下に晒した場合に炭酸成分の一部が容器外に出るおそれがあり、かかる炭酸ガスが出た場合、医療用溶液の安全性が失われる。そこで、上記ガスバリアー性の包装材で真空包装すると、使用時に高温化に晒された医療用容器が炭酸ガスを容器外に放出した場合、包装材内に炭酸ガスが溜まり、使用直前に安全性を欠いた医療用容器の認識が容易にでき、医療用容器の危険な使用を避けることができる。

【００１４】具体的なガスバリアー性包装体としては、包装壁が殆ど、又は全くガスを透過させないアルミニウム等の金属層、またポリ塩化ビニリデン、ポリエステル、ナイロン、エチレン-ビニルアルコール共重合体、フッ素系樹脂等のようにガスバリアー性の高い樹脂層、又はアルミニウム、珪素、マグネシウム、チタン、銀、金等の土類金属若しくは金属、又はその酸化物の蒸着層等を有するものである。包装体におけるガスバリアー性層の酸素透過量は４０ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ（温度：２０℃）以下、特に、３０ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ以下、また好ましくは５ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ以下、更には１ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ以下であることが望ましい。包装体におけるガスバリアー性層の炭酸ガス透過量は、２００ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ（温度：２５℃）以下、特に、１００ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ以下、また好ましくは１０ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ以下、更には１ｃｃ・２０μ／m^2・ｄａｙ・ａｔｍ以下であることが望ましい。

【００１５】

【実施例】以下、本発明に係る炭酸成分入り医療用容器の好ましい実施例を添付図面を参照しながら詳述する。図１は本発明に係る炭酸成分入り医療用容器における第一実施例の平面図である。図２は第一実施例の医療用容器の使用時の平面図である。本実施例に係る炭酸成分入り医療用容器１は一の室２に重炭酸から成る炭酸成分溶液３を液密に収容し、他の室５に炭酸成分以外の電解質からなる母液６を液密に収容した多室容器からなり、使用時に上記各室２、３同士を連通して炭酸成分溶液３と母液６とを混合して炭酸成分入り医療用溶液９が提供される医療用容器である。医療用容器１は上記混合後の医療用溶液９中に重炭酸イオン量が１０～３５ｍｍｏｌ／Ｌの範囲で含まれるように上記一の室２に炭酸成分が収容され、上記混合後の医療用溶液９中に上記炭酸成分の一部が１０～８０ｍｍＨｇの範囲で炭酸（炭酸イオン及び炭酸ガス）が生じるように上記他の室５の母液６に過剰酸が含まれている。

【００１６】第一実施例に係る炭酸成分入り医療用容器１を更に詳しく説明すると、医療用容器１はブロー成形物からなり、ブロー成形物の胴壁の厚みは２５０μｍで、その容量は１６００ｍｌで、長さが５００ｍｍで、幅が２００ｍｍである。ブロー成形物の胴壁は外層と内層との二層に成形され、外層は厚みが２２０μｍの直鎖状低密度ポリエチレン（密度：０．９３５ｇ／cm^3、ＭＩ：２、融点：１２１℃）からなる。内層は厚みが３０μｍの直鎖状低密度ポリエチレン（密度：０．９３５ｇ／cm^3、融点：１２１℃）とポリプロピレン（密度：０．９００ｇ／cm^3、ＭＩ：０．７、融点：１６５℃）とを２：１の割合で混合したブレンド物の層からなる。ブロー成形物はブロー成形時のブロー吹出口が医療用容器１における排出用ポート８として形成され、対向端部に混注用ポート７が形成されている。医療用容器１の胴部には容器１内を二室に分ける接着シール部４、４が形成されている。接着シール部４、４は内壁同士が液密に接着シールされて形成され、接着シール部４、４は剥離可能なピールシールである。接着シール部の剥離強度は、一の室２内の圧が０．０１～０．０３Ｋｇｆ／cm^2の昇圧で剥離する強度である。

【００１７】接着シールで隔離される医療用容器１の一の室２には炭酸成分溶液３が収容され、他の室５には母液６が収容される。炭酸成分溶液３には炭酸水素ナトリウム２６ｍｍｏｌが水５００ｍｌに含有され、母液には、塩化ナトリウム１０２ｍｍｏｌ、塩化カリウム４ｍｏｌ、塩化カルシウム１．５ｍｏｌ、グルコース４０ｇ及び過剰酸として乳酸２．５ｍｍｏｌが水５００ｍｌに含有されている。次に、第一実施例の医療用容器１の製造方法について説明すると、ブロー成形により医療用容器１の本体を作製し、接着シール部４、４を形成した後、各室２、５内を洗滌、乾燥する。次に、混注用ポート７から上記炭酸成分溶液３を収容室２に充填し、混注用ポート７をゴム栓で液密に密封する。排出用ポート８から上記母液６を収容室５に充填し、排出用ポート８をゴム栓で液密に密封する。密封後、温度１１０℃で高圧蒸気滅菌処理する。高圧蒸気滅菌処理の際にはオートクレーブ内を窒素と共に炭酸ガス１００ｍｍＨｇの雰囲気で行う。冷却後、これを医療用容器１とする。かかる第一実施例の医療用容器１を１０サンプル製造し、図２に示す如く接着シール部４、４を剥離して上記炭酸成分溶液３及び母液６を混合し、その混合医療用溶液１中のＰＨ値及び総炭酸量の測定から該溶液１中の重炭酸イオン量及び炭酸ガス量を求めその結果を表１に示した。

【００１８】

【表１】

実施例１ サンプルＮｏ	重炭酸イオン量 (m mol/L)	炭酸ガス量 (mmHg)	ＰＨ値
1	22.9	52	7．27
2	23.2	57	7．28
3	23.3	61	7．20
4	23.5	66	7．17
5	23.8	51	7．29
6	23.1	53	7．26
7	23.4	59	7．22
8	23.5	55	7．25
9	23.0	54	7．25
10	23.2	54	7．26

【００１９】上記表１の結果から医療用容器１内の医療用溶液９は重炭酸イオン濃度及び炭酸ガス量がほぼ血漿中に近い状態で得られることが分かる。またサンプルのばらつきも許容されるものである。また、上記医療用容器１では各溶液３、６の分注誤差も製造上少なく、また蒸気滅菌時の炭酸ガスの喪失も許容範囲内であることが分かる。

【００２０】次に、本発明に係る医療用容器の第二実施例について説明する。図３は本発明に係る医療用容器の

第二実施例の平面図である。図３に示す如く第二実施例に係る医療用容器１１は第一実施例に係る医療用容器１とほぼ同様な構成からなるが、異なる点は以下の点にある。上記炭酸成分溶液１３には重炭酸ナトリウム２６ｍｍｏｌ及び水酸化ナトリウム５ｍｍｏｌが５００ｍＬ含有されている。母液１６には、塩化ナトリウム１０２ｍｍｏｌ、塩化カリウム４ｍｏｌ、塩化カルシウム１．５ｍｏｌ、グルコース４０ｇ及び過剰酸として塩酸５．０ｍｍｏｌ、及び酢酸１．５ｍｍｏｌが水５００ｍｌに含有されている。また医療用容器１１は通常の蒸気滅菌処理した後に包装体２１で上記炭酸成分溶液１３の収容室２の部分が真空密封包装されている。包装体２１は低密度ポリエチレン層：５０μｍ／エチレン・ビニルアルコール共重合体層：２０μｍ／低密度ポリエチレン層：５０μｍからなり、炭酸ガス透過量が０．８１cc／m^2・24hr（温度２５℃、DRY）以下のガスバリアー性シートからなる。かかる第二実施例の医療用容器１１を第一実施例と同様に１０サンプル製造し、１カ月間室温で保存した後に接着シール部４、４を剥離して上記炭酸成分溶液１３及び母液１６を混合し、その混合医療用溶液中のＰＨ値及び総炭酸量の測定から該溶液中の重炭酸イオン量及び炭酸ガス量を求めその結果を表２に示した。

【００２１】

【表２】

実施例２ サンプルＮｏ	重炭酸イオン量 (m mol/L)	炭酸ガス量 (mmHg)	ＰＨ値
1	24.5	41	７．４０
2	24.5	42	７．３９
3	24.2	44	７．３７
4	24.6	43	７．３８
5	24.6	41	７．４０
6	24.4	45	７．３６
7	24.0	48	７．３２
8	24.2	42	７．３８
9	24.4	47	７．３４
１０	24.1	46	７．３４

【００２２】上記表２の結果から医療用容器１１内の医療用溶液は重炭酸イオン濃度及び炭酸ガス量が血漿中と同様な状態で得られることが分かる。またサンプルのばらつきも殆ど無かった。また蒸気滅菌時の炭酸ガスの喪失も殆ど無かった。上記実施例では、輸液剤の組成を用いたが、臓器保存液等に用いても良い。上記実施例では、輸液剤の母液を一の収容室５に収容したが、アミノ酸と糖とを含むものについては母液収容室５を更に２以上の室に分けても良い。上記実施例では、ブロー成形物から容器本体を成形したが、可撓性で透明性を有する限り、インフレーション樹脂シート、射出成形物、真空成形物等であっても良い。上記実施例では、収容室は容器を区分して形成したが、別別の容器を接続させて形成しても良く、また、無菌的連通手段は剥離可能な接着シール部である必要はない。

【００２３】

【発明の効果】以上説明したように本発明に係る炭酸成分入り医療用容器によれば、上記混合後の医療用溶液中に重炭酸イオン量が１０～３５ｍｍｏｌ／Ｌの範囲で含まれるように上記一の室に上記炭酸成分が収容され、上記混合後の医療用溶液中に上記炭酸成分の一部が炭酸（炭酸イオン及び炭酸ガス）を１０～８０ｍｍＨｇの範囲で生じるように上記他の室の母液に過剰酸が含まれているので、製造前、製造後、或いは長期保存後のどの段階であってもＰＨ値がほぼ一定に維持され、且つ炭酸ガス濃度も一定に維持される炭酸成分入り医療用溶液を収容することができる。

【図面の簡単な説明】

【図１】図１は本発明に係る炭酸成分入り医療用容器における第一実施例の平面図である。

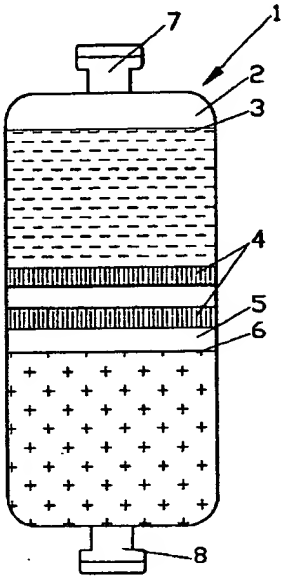
【図２】図２は第一実施例の医療用容器の使用時の平面図である。

【図３】図３は本発明に係る医療用容器の第二実施例の平面図である。

【符号の説明】

1	医療用容器
2	一の室
3	炭酸成分溶液
4	接着シール部
5	他の室
6	母液
9	医療用溶液

【図１】



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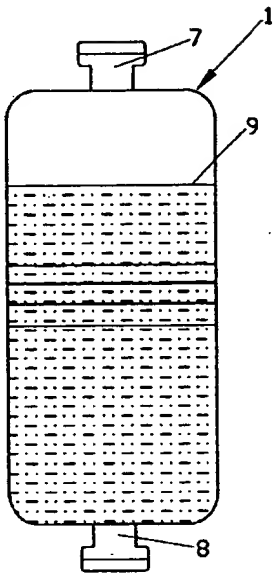

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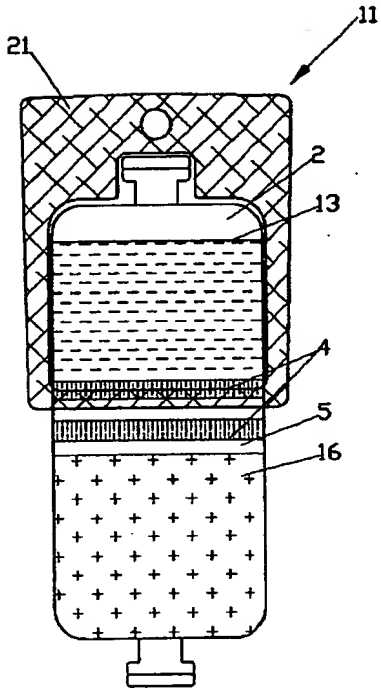

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R : Japanese Laid-Open Publication No. 11-9659

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Inventor: Hiroshi MOTOBAYASHI
Applicant: Shinsozai Sogo Kenkyusho K.K.

[Title of the Invention] MEDICAL CONTAINER

[Claims]

[Claim 1] A medical container consisting of a multichamber container comprising a chamber fluid-tightly containing a carbonic acid component solution consisting of bicarbonate or carbonic acid and another chamber fluid-tightly containing a mother liquid consisting of an electrolyte other than the carbonic acid component, wherein the chambers communicate with each other for use so that the carbonic acid component solution and the mother liquid are mixed with each other so as to provide a medical solution containing a carbonic acid component, and wherein:

the carbonic acid component is contained in the first chamber so that the medical solution after the mixing contains an amount of bicarbonate ions ranging from 10 to 35 mmol/L; and

the mother liquid in the second chamber contains an excess of acid, so that after mixing a portion of the carbonic acid component generates carbonic acid (carbonate ions and carbonic acid gas) in the medical solution in an amount ranging from 10 to 80 mmHg.

[Claim 2] A medical container according to claim 1, wherein: an excessive alkali salt (B) is added to th car-

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bonic acid compon nt solution for preventing decomposition loss of the carbonic acid component during storage thereof; and the excessive acid is added to the mother liquid so that 0.5 mEq/L ≤ excessive acid (A) - excessive alkali salt (B) ≤ 5.0 mEq/L.

[Claim 3] A medical container according to claim 2, wherein at least the first chamber is packaged with a package material having a gas-barrier property.

[Claim 4] A medical container according to claim 3, wherein the packaging with the package material is vacuum packaging.

[Detailed Description of the Invention]

[0001]

[Field of the Invention] The present invention relates to a medical container containing an infusion solution, a dialysis solution, an organ preserving solution, or the like and, more particularly, to a medical container containing a medical solution which contains an unstable carbonic acid component.

[0002]

[Prior Art] Generally, when sodium bicarbonate is contained in a resin container, or the like, the sodium bicarbonate decomposes while being heated or stored, thereby generating carbonic acid gas, which passes through the container wall and is lost. By such decomposition, [OH^-] increases in the solution for ionization equilibrium, thereby increasing the pH value of the solution. In order to store such medical containers for a long period of time, a technique has been suggested (Japanese Patent No. 2527532, Japanese Laid-Open Publication No. 6-105905) which prevents the carbonic acid gas in the resin container from coming out of th resin container by providing a carbonic acid gas atmosphere around a

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medical container by seal-packaging the medical container with a package having a gas-barrier property and introducing a carbonic acid gas into the package or by providing in the package an oxygen scavenger of a type which generates carbonic acid gas.

[0003]

[Problems to be Solved by the Invention] However, the conventional method for producing a medical container containing a carbonic acid component has the following problems. For those containing a carbonic acid gas within the package or those provided with an oxygen scavenger, the initial pH value of the solution in the medical container is as high as 8.32 or 8.60 in view of the loss of carbonic acid ion during a steam sterilization process. Then, after 10 days, the pH value in the medical container becomes 8.0 or less. It is believed that this occurs because some of the solution in the medical container is present within the package and receives the carbonic acid gas passing through the container wall. The solution in such a medical container will have a composition which is apparently different from the initial composition thereof; it is unknown how much of the carbonic acid gas is dissolved in the solution in the medical container. A solution which has received an excessive amount of carbonic acid gas may react with calcium ion and/or magnesium ion in the solution, thereby producing precipitation. In view of the above, the present invention has been made to provide a medical container containing a medical solution which contains a carbonic acid component, in which the pH value is kept at a substantially constant level while the carbonic acid gas concentration is also kept at a constant level, at any stage, including before production, after production or after long-term storage.

[0004]

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[Means for Solving the Problems] The present invention provides a medical container consisting of a multichamber container comprising a chamber fluid-tightly containing a carbonic acid component solution consisting of bicarbonate or carbonic acid and another chamber fluid-tightly containing a mother liquid consisting of an electrolyte other than the carbonic acid component, wherein the chambers communicate with each other for use so that the carbonic acid component solution and the mother liquid are mixed with each other so as to provide a medical solution containing a carbonic acid component, and wherein: the carbonic acid component is contained in the first chamber so that the medical solution after the mixing contains an amount of bicarbonate ions ranging from 10 to 35 mmol/L; and the mother liquid in the second chamber contains an excess of acid, so that after mixing a portion of the carbonic acid component generates carbonic acid (carbonate ions and carbonic acid gas) in the medical solution in an amount ranging from 10 to 80 mmHg, thereby achieving the above-described object.

[0005] The medical container is normally a resin container having a flexible wall. The flexible wall may be any wall as long as it is flexible so that the volume of the container can easily change. The container wall preferably has a level of transparency such that the contents of the container can be visually checked. Such transparency may be necessary to check the state of the drug within the container. The container may be formed by molding, extrusion molding, injection molding, or blow molding from an inflation film, a tube, a sheet or a film. The resin material for a resin container may be any general-purpose resin, such as a polyolefin-based resin, vinyl chloride, a vinylidene chloride-based resin, a polyester-based resin, a polyvinyl alcohol-based r sin, a polyacrylonitril -bas d resin, a polyacrylic acid-based resin, or a polyamide-based resin.

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Moreover, the resin container may b in a single layer form or a multi-layer form. The innermost layer being in contact with the drug contained in the resin container is preferably a resin layer which does not affect the drug or produce an elute. While such a resin is preferably a polyolefin-based resin, the resin may be other resins, including, for example, lower-olefin resins such as low-, intermediate- and high-density polyethylene, polypropylene, etc. Moreover, the resin container wall is preferably provided with a layer having a gas-barrier property. Particularly, a layer which does not easily pass oxygen, or the like, is preferred. Such a layer having a gas-barrier property includes a metal layer of aluminum, or the like, or an inorganic deposited layer of silicon oxide, magnesium oxide, titanium oxide, or the like, which does not substantially or does not at all pass a gas therethrough; or a resin layer having a high gas-barrier property of polyvinylidene chloride, polyester, nylon, an ethylene-vinylalcohol copolymer, a fluorine-based resin, or the like. The amount of oxygen passed through the layer having a gas-barrier property is 40 cc•20μ/m^2•day•atm (temperature: 20° C) or less; preferably, 30 cc•20μ/m^2•day•atm or less; more preferably, 5 cc•20μ/m^2•day•atm or less; and even more preferably, 1 cc•20μ/m^2•day•atm or less. Moreover, the wall of the resin container preferably has a level of transparency such that the drug contained therein can be visually checked. Thus, the wall made of a metal layer such as the above-described aluminum layer having a desirable function of passing no gas therethrough is preferably peelable at least in a portion of the metal layer. With a resin container having such a layer, it is possible to sufficiently prevent the drug contained therein from deteriorating due to heat during a high pressure steam sterilization process.

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[0006] The carbonic acid component and a mother liquid are separately and fluid-tightly charged and subjected to a steam sterilization process. For separately and fluid-tightly containing the carbonic acid component solution and the mother liquid, a resin-made container may be used which has a plurality of chambers for individually containing the carbonic acid component solution and the mother liquid. When such a container is divided into a plurality of chambers, a chamber-partitioning portion is preferably provided with communication means for communicating the chambers to each other by an operation via the container wall. Such communication means may be provided by: using closed tubes each having one end which can be broken via the container wall to communicate the tubes to each other; clamping the partitioning portion with a clamping clip, or the like; providing the partitioning portion by a peel-seal portion which can be peeled by an external operation; or using any other means which allows for an aseptic communication operation. It is also possible to use a plurality of separate containers containing the carbonic acid component and the mother liquid, respectively, and to connect the containers to each other, whereby the individual containers are used as chambers. Connection between the containers may be provided by: using the above-described peel-seal portion at an end of each of the containers and connecting the respective ends of the containers together, so that the containers can be communicated to each other before use by an operation via the container; by connecting the containers to each other by communication means comprising a communication needle which per se is known in the art so that the containers can be communicated to each other by an operation of the communication means. When the container comprises a plurality of containers, at least one of the containers may be a glass container, though both of the containers are preferably resin-mad contain rs. Preferably, th chambers of the con-

tainer are each formed of, or connected to each other via, a peel-seal portion so that the containers can be communicated to each other via the container or via the package.

[0007] The peel-seal portion is also called a weak seal portion and it is a partitioning seal portion which is peeled off when the inside of the container reaches a certain pressurized state. The peeling strength of the peel-seal portion is preferably such that the peel-seal portion is peeled off by an increase in the internal pressure of the chamber of 0.01-1.0 kgf/cm^2 and, more preferably, 0.05-0.5 kgf/cm^2. A strength below this range will result in insufficient safety to keep the chambers separated during production, shipping and storage of the container. When the strength is above this range, the operation of communicating the chambers to each other before use may not be facilitated. In order to provide a peel-seal or a complete secure seal between the inner layers of the resin container, any technique which per se is known in the art may be used. In order to ensure that these seals are different from each other, the inner layer of the resin container is preferably a blend of different resins. Preferably, the resin blend is made of resins which are different from one another in the thermal melting temperature or the Vicat softening point, and which have small compatibility with each other. By having such a blend layer, the seal temperature to achieve completely sealed bonding can be easily set using the same inner layer, while the seal temperature to achieve peel-seal bonding can also be easily set. Moreover, it is possible to exactly determine the seal strength required for the peel-seal bonding, i.e., the relationship between the capability of being easily peeled off by an external force before use and the seal strength such that the seal is not peeled off during storage. In particular, a r sin having a different compatibility from that of th inner layer is melted and mixed with the inner

layer, which is then shaped in a sheet form, thereby obtaining a surface which is separated into portions with microscopically different thermobonding properties. The thermal melting properties for the respective microscopic portions on the surfaces of the sheet at a temperature can be determined so as to accurately define the seal strength, thereby easily achieving the above-described effect.

[0008] The mother liquid may be a component used in an infusion solution, a dialysis solution, or an organ preserving solution, including: an inorganic electrolyte which is present in a human body, such as sodium, potassium, magnesium, calcium, chlorine, phosphorus, and the like: and an organic electrolyte which is present in the human body such as acetic acid, lactic acid, citric acid, and the like. In addition to the electrolytes, the mother liquid may also include an energy such as saccharide, amino acid, protein, fat, and optionally physiologically active substances, vitamins, and the like. While the mother liquid may be aseptically charged into the resin container, preferably, it is first fluid-tightly contained in the chamber of the resin container and then subjected to a steam sterilization process. This is because such a sterilization process ensures sterility of the mother liquid which can then be safely administered to the patient. The carbonic acid component solution in the first chamber is obtained by dissolving a bicarbonate or a carbonate therein so that the amount of bicarbonate ion in the mixed medical solution is in the range of 10-35 mmol/L, preferably, 15-30 mmol/L and, more preferably, 20-28 mmol/L. It is believed that the concentration of the bicarbonate ion in blood plasma is normally 22-26 mEq/L, and it is thus preferred that the medical solution contains bicarbonate ion in such a normal range. However, a dose range wid r than the normal rang may be acceptabl since the administration of an infusion agent, or the like, is temporary.

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Moreover, the carbonic acid component solution preferably contains an alkali salt such as sodium or potassium in an amount equal to or greater than the amount of bicarbonate ion which is the carbonic acid component. When such an amount of alkali salt is contained, the inside of the first chamber is maintained to be alkaline since carbonic acid is a weak acid, and it is possible to suppress, as much as possible, the carbonic acid component from coming out of the container as carbonic acid gas and being lost. The volume of the above-described carbonic acid component solution is preferably 1/10-1/1 of the volume of the mother liquid. When the volume of the carbonic acid component solution is decreased below this range, a charging error increases, thereby impeding the production line.

[0009] An excessive acid is contained in the mother liquid in the second chamber so that a portion of the carbonic acid component generates an amount of carbonic acid (carbonic acid ion and carbonic acid gas) in the range of 10-80 mmol/L in the mixed medical solution. Normally, various positive and negative ions, {OH^-, X^-, Y^-, Z^-, ...} and {H^+, A^+, B^+, C^+, ...}, are present in the solution while being dissociated because the mother liquid is an electrolyte solution. When the pH value is around 7, the respective amounts of positive and negative ions, {X^-, Y^-, Z^-, ...} and {A^+, B^+, C^+, ...}, are equal to each other, excluding the hydrogen ions and the hydroxyl ions. However, when the negative electrolyte is provided in excess of the positive electrolyte, the amount of excessive negative electrolyte ion ≈ {X^-, Y^-, Z^-, ...} - {A^+, B^+, C^+, ...}, whereby the pH value decreases to maintain the equilibrium between the negative electrolyte ion and the hydrogen ion [H^+] in the solution. This is the excessive acid state. For such a mother liquid in which xcessiv acid is pr sent, when a carbonic acid component consisting of, for example, 25.5 mmol/L of sodium

bicarbonate is mixed in such a mother liquid having 1.0 mEq/L of excessive acid, carbonic acid gas and carbonic acid ion will be generated. While 25 mmol/L of sodium ion has an equilibrium relationship with the bicarbonate ion before the mixing, only 1 mEq/L of excessive acid has an ionization relationship in the medical solution after the mixing, because bicarbonate is a weaker acid than hydrochloric acid, lactic acid, acetic acid, and the like, that are also present in the mother liquid. When the pH value of the mixed medical solution is kept around 7 due to the buffering effect of the other electrolytes, 1 mmol of [HCO_3^-] in 25 mEq/L of bicarbonate ion is bound to [H^+], and is dissolved in the solution as carbonic acid gas or partially released to the outside of the container, because both of the hydroxyl ions and the hydrogen ions are present on a nano order. Therefore, the amount of the bicarbonate ion in the mixed medical solution is 24 mEq/L, and carbonic acid gas is generated in the medical solution, a part or all of which is then dissolved therein. The carbonic acid gas contributes to the pH value of the solution according to the following Henderson-Hasselbalch equation: pH value=6.1+log[HCO_3^-]/0.03×(pCO_2)].

[0010] In the medical container of the present invention, a carbonic acid gas is generated in the mixed medical solution in an amount ranging from 10 to 80 mmHg. Therefore, theoretically, the excessive acid is contained in the range from 80×0.03 mEq/L to 10×0.03 mEq/L, that is, 2.4-0.3 mEq/L. However, for the excessive acid, not all of the carbonic acid gas is dissolved in the mixed solution, but some of the carbonic acid gas is also released to the atmosphere. The amount of carbonic acid gas to be released depends upon the amount of carbonic acid generated. About 50% of the carbonic acid gas is released for the range of 100 mmHg-200 mmHg, and about 40% for the range of 50 mmHg-90 mmHg.

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Thus, in view of such an amount, the excessive acid can be present in the range of 0.5-5 mEq/L and, preferably, 1.0-2.4 mEq/L. The carbonic acid concentration in the mixed medical solution of the present invention is obtained from the above-described Henderson-Hasselbalch equation. The excessive acid is an acid intended to generate carbonic acid in the mixed medical solution. For example, when the first chamber for the carbonic acid component does not contain bicarbonate ion and a corresponding amount of a salt of sodium, or the like, i.e., when sodium hydroxide, or the like, is added to increase the alkalinity of the carbonic acid component, and an amount of alkali salt (B) in excess of the bicarbonate ion is contained therein, then, an amount of acid, e.g., hydrochloric acid, which is equivalent to that of such an excessive alkali salt is added to the amount of excessive acid which is contained in the mother liquid for the purpose of generating the carbonic acid gas.

[0011] With the medical container containing a carbonic acid component of the present invention having such a structure, it is not necessary, after production, to absorb or supply a carbonic acid gas, or the like, whereby the medical solution will not be altered. Moreover, simply by communicating the chambers to each other before use, a carbonic acid gas is generated in the medical solution, whereby it is possible to maintain a composition that is substantially the same as that of a body fluid. Particularly, it is possible to provide an amount of bicarbonate ion and an amount of carbonic acid gas which are close to those in blood plasma, so as to provide a pH value which is close to that of blood plasma. Thus, lactic acidosis, or the like, will not be caused as in the prior art.

[0012] Claim 2 of the present invention is directed to a medical contain r according to claim 1, wherein: an exces-

sive alkali salt (B) is added to the carbonic acid component solution for preventing decomposition loss of the carbonic acid component during storage thereof; and the excessive acid is added to the mother liquid so that 0.5 mEq/L ≤ excessive acid (A) - excessive alkali salt (B) ≤ 5.0 mEq/L. When the excessive alkali salt (B) is added to the carbonic acid component solution contained in the first chamber, it is possible to suppress, as much as possible, the carbonic acid component from being decomposed and coming out of the chamber. Normally, the carbonic acid component becomes more likely to be decomposed by the heating during the high pressure steam sterilization process for the medical container. A portion of the carbonic acid component may also be lost as carbonic acid gas when the container is inadvertently exposed to a high temperature during storage. However, a carbonic acid component solution in which an amount of alkali salt (B) is present in excess of the amount of bicarbonate ion prevents the portion of the carbonic acid component from being released as carbonic acid gas.

[0013] Claim 3 of the present invention is directed to a medical container according to claim 2, wherein at least the first chamber is packaged with a package material having a gas-barrier property. The entire medical container, or only the first chamber, may be packaged with a package material having a gas-barrier property. When the excessive alkali salt (B) is present in the first chamber, atmospheric carbonic acid gas may be absorbed via the container during storage thereof. Then, the amount of the carbonic acid component changes during the storage, which poses a problem in terms of the safety of the medical solution. However, by packaging the first chamber with the package material having a gas-barrier property, no atmospheric carbonic acid gas is absorbed. Claim 4 of the present invention is directed to a medical container according to claim 3, wherein the packag-

ing with the package material is vacuum packaging. When the container is inadvertently exposed to a high temperature during storage, a portion of the carbonic acid component may come out of the container. When the carbonic acid gas comes out, the safety of the medical solution is lost. When the medical container is vacuum-packaged with the package material having a gas-barrier property, even if the medical container is exposed to a high temperature in use to release a carbonic acid gas to the outside of the container, the carbonic acid gas is collected in the package material. Thus, a medical container lacking safety can easily be checked before use thereof, and the dangerous use of such a medical container can be avoided.

[0014] Specifically, the package having a gas-barrier property includes: a metal layer such as an aluminum layer which does not substantially or does not at all pass a gas therethrough; or a resin layer having a high gas-barrier property of polyvinylidene chloride, polyester, nylon, an ethylene-vinylalcohol copolymer, a fluorine-based resin, or the like; a deposited layer of an earth metal, a metal or an oxide thereof such as aluminum, silicon, magnesium, titanium, silver, or gold; and the like. The amount of oxygen passed through the layer having a gas-barrier property in the package is 40 cc•20μ/m²•day•atm (temperature: 20°C) or less; preferably, 30 cc•20μ/m²•day•atm or less; more preferably, 5 cc•20μ/m²•day•atm or less; and even more preferably, 1 cc•20μ/m²•day•atm or less. The amount of carbonic acid gas passed through the layer having a gas-barrier property in the package is 200 cc•20μ/m²•day•atm (temperature: 25°C) or less; preferably, 100 cc•20μ/m²•day•atm or less; more preferably, 10 cc•20μ/m²•day•atm or less; and even more preferably, 1 cc•20μ/m²•day•atm or less.

[0015]

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[Examples] Hereinafter, a medical container containing a carbonic acid component according to preferred examples of the present invention will be described in detail with reference to the accompanying drawings. Figure 1 is a plan view illustrating a medical container containing a carbonic acid component according to the first example of the present invention. Figure 2 is a plan view illustrating the medical container of the first example in use. A medical container 1 containing a carbonic acid component according to the present example comprises a chamber 2 fluid-tightly containing a carbonic acid component solution 3 consisting of bicarbonate and another chamber 5 fluid-tightly containing a mother liquid 6 consisting of an electrolyte other than the carbonic acid component, wherein the chambers 2, 3 are communicated with each other for use so that the carbonic acid component solution 3 and the mother liquid 6 are mixed with each other so as to provide a medical solution 9 containing a carbonic acid component. In the medical container 1, the carbonic acid component is contained in the first chamber 2 so that the medical solution 9 after the mixing contains an amount of bicarbonate ions ranging from 10 to 35 mmol/L; and the mother liquid 6 in the second chamber 5 contains an excess of acid, so that after mixing a portion of the carbonic acid component generates carbonic acid (carbonate ions and carbonic acid gas) in the medical solution 9 in an amount ranging from 10 to 80 mmHg.

[0016] The medical container 1 containing the carbonic acid component according to the first example will be described in greater detail. The medical container 1 is made from a blow-molded product whose body wall has a thickness of 250 μm, a volume of 1600 ml, a length of 500 mm, and a width of 200 mm. The body wall of the blow-molded product is formed in two layers, comprising an outer layer and an inn r layer. The outer layer is made of linear low density poly-

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ethylene (density: 0.935 g/cm^3, MI: 2, melting point: 121°C) having a thickness of 220 μm. The inner layer is made of a blend product of linear low density polyethylene (density: 0.935 g/cm^3, melting point: 121°C) and polypropylene (density: 0.900 g/cm^3, MI: 0.7, melting point: 165°C) being mixed with each other at a ratio of 2:1. A port on one side of the blow-molded product used as a blowing port during the blow-molding process is used as a discharge port 8 of the medical container 1, with a mixed injection port 7 being formed on the other side of the container. Adhesion seal portions 4, 4 for dividing the container 1 into two chambers are provided in the body portion of the medical container 1. The adhesion seal portions 4, 4 are formed by fluid-tightly adhesion-sealing the inner walls together, and the adhesion seal portions 4, 4 are peel seals which can be peeled off. The peeling strength of the adhesion seal portion is such that the peel-seal portion is peeled off by an increase in the internal pressure of the first chamber 2 of 0.01-0.03 kgf/cm^2.

[0017] The medical container 1 is divided by the adhesion seals into the first chamber 1 which contains the carbonic acid component solution 3 and the second chamber 5 which contains the mother liquid 6. The carbonic acid component solution 3 contains 26 mmol of sodium bicarbonate in 500 ml of water, whereas the mother liquid contains, in 500 ml of water, 102 mmol of sodium chloride, 4 mol [sic] of potassium chloride, 1.5 mol [sic] of calcium chloride, 40 g of glucose, and 2.5 mmol of lactic acid as excessive acid. Next, a method for producing the medical container 1 of the first example will be described. The main body of the medical container 1 is first produced by blow molding, and the adhesion seal portions 4, 4 are then formed therein, after which the inside of each of the chambers 2 and 5 is washed and dried. Th n, the carbonic acid component solution 3 is

charged into the container chamber 2 through the mixed injection port 7, and the mixed injection port 7 is fluid-tightly sealed with a rubber stopper. The mother liquid 6 is charged into the container chamber 5 through the discharge port 8, and the a discharge port 8 is fluid-tightly sealed with a rubber stopper. After the sealing, the container is subjected to a high pressure steam sterilization process at a temperature of 110° C. The high pressure steam sterilization process is performed in an atmosphere in an autoclave containing nitrogen and 100 mmHg of carbonic acid gas. After cooling, the medical container 1 is obtained. Ten samples of medical containers 1 of the first example were produced. The adhesion seal portions 4, 4 were peeled off, as illustrated in Figure 2, so as to mix the carbonic acid component solution 3 and the mother liquid 6 with each other. The amount of bicarbonate ion and the amount of carbonic acid gas in the mixed medical solution 1 were obtained by measuring the pH value and the total amount of carbonic acid in the solution 1. The results are shown in Table 1.

[0018]

[Table 1]

Example1 Sample No	Amount of bicarbonate ion (m mol/l)	Amount of carbonic acid gas (mmHg)	pH value
1	22.9	52	7.27
2	23.2	57	7.23
3	23.3	61	7.20
4	23.6	68	7.17
5	23.8	51	7.29
6	23.1	53	7.26
7	23.4	59	7.22
8	23.6	55	7.26
9	23.0	54	7.25
10	23.2	54	7.26

[0019] From the results shown in Table 1, it can b seen that the medical solution 9 in the medical container 1 has a bicarbonate ion concentration and an amount of carbonic acid

gas which are substantially the same as those in blood plasma. Moreover, the variation among the samples is acceptable. It can also be seen that in the production of the medical container 1, there is only a small error in the divided injections of the solutions 3 and 6, and the loss of carbonic acid gas during the steam sterilization process is within an acceptable range.

[0020] Next, a medical container according to the second example of the present invention will be described. Figure 3 is a plan view illustrating the medical container according to the second example of the present invention. As illustrated in Figure 3, a medical container 11 of the second example has substantially the same structure as that of the medical container 1 of the first example, only with the following difference. Each 500 mL of the carbonic acid component solution 13 contains 26 mmol sodium bicarbonate and 5 mmol sodium hydroxide. The mother liquid 16 contains, in 500 ml of water, 102 mmol of sodium chloride, 4 mol of potassium chloride, 1.5 mol of calcium chloride, 40 g of glucose, 5.0 mmol of hydrochloric acid as excessive acid, and 1.5 mmol of acetic acid. After the medical container 11 is subjected to an ordinary steam sterilization process, the chamber 2 containing the carbonic acid component solution 13 is vacuum-seal-packaged with a package 21. The package 21 is made of a sheet with a gas-barrier property which passes 0.81 cc/m^2•24hr (temperature: 25°C, dry) or less of carbonic acid gas. The sheet comprises low density polyethylene: 50 μm/ethylene-vinylalcohol copolymer: 20 μm/low density polyethylene: 50 μm. As in the first example, 10 samples of medical containers 11 according to the second example were produced, and stored at room temperature for one month. Then, the adhesion seal portions 4, 4 were peeled off so as to mix the carbonic acid component solution 13 and the moth r liquid 16 with each other. The amount of bicarbonate

ion and the amount of carbonic acid gas in the mixed medical solution were obtained by measuring the pH value and the total amount of carbonic acid in the solution. The results are shown in Table 2.

[0021]

[Table 2]

Example 2 Sample No	Amount of bicarbonate ion (mmol/l)	Amount of carbonic acid gas (mmHg)	pH value
1	24.5	41	7.40
2	24.5	42	7.38
3	24.2	44	7.37
4	24.6	43	7.38
5	24.6	41	7.40
6	24.4	45	7.36
7	24.0	48	7.32
8	24.2	42	7.38
9	24.4	47	7.34
10	24.1	46	7.34

[0022] From the results shown in Table 2, it can be seen that the medical solution in the medical container 11 has a bicarbonate ion concentration and an amount of carbonic acid gas which are substantially the same as those in blood plasma. Moreover, there was substantially no variation among the samples. Furthermore, there was substantially no loss of carbonic acid gas during the steam sterilization process. In the illustrated examples, an infusion agent composition was used, but an organ preserving solution may alternatively be used. In the illustrated examples, the mother liquid of the infusion agent was contained in the first container chamber 5, but the mother liquid chamber 5 may be further divided into two or more chambers when the mother liquid contains amino acid and saccharide. In the illustrated examples, the container body was molded from a blow-molded product, but the container body may alternatively be an inflation resin she t, an injection-molded product, a vacuum-molded product, or the like, as long as it

has flexibility and transparency. In the illustrated examples, the container chambers were obtained by partitioning a container, but separate containers may alternatively be connected together. Moreover, the aseptic communication means does not have to be a peelable adhesion seal portion.

[0023]
[Effects of the Invention] As described above, in a medical container containing a carbonic acid component according to the present invention, the carbonic acid component is contained in the first chamber so that the medical solution after the mixing contains an amount of bicarbonate ions ranging from 10 to 35 mmol/L; and the mother liquid in the second chamber contains an excess of acid, so that after mixing a portion of the carbonic acid component generates carbonic acid (carbonate ions and carbonic acid gas) in the medical solution in an amount ranging from 10 to 80 mmHg. Thus, the container can contain a medical container which contains a carbonic acid component, so that the pH value is kept at a substantially constant level while the carbonic acid gas concentration is also kept at a constant level, at any stage, including before production, after production or after long-term storage.

[Brief Description of the Drawings]
[Figure 1] Figure 1 is a plan view illustrating a medical container containing a carbonic acid component according to the first example of the present invention.

[Figure 2] Figure 2 is a plan view illustrating the medical container of the first example in use.

[Figure 3] Figure 3 is a plan view illustrating a medical container according to the second example of the present invention.

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[Description of the Reference Numerals]

1 Medical container
2 First chamber
3 Carbonic acid component solution
4 Adhesion seal portion
5 Second chamber
6 Mother liquid
9 Medical solution

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[Abstract]

[Objective] To provide a medical container containing a medical solution which contains a carbonic acid component, in which the pH value is kept at a substantially constant level while the carbonic acid gas concentration is also kept at a constant level, at any stage, including before production, after production or after long-term storage.

[Structure] A medical container consisting of a multichamber container comprising a chamber fluid-tightly containing a carbonic acid component solution consisting of bicarbonate or carbonic acid and another chamber fluid-tightly containing a mother liquid consisting of an electrolyte other than the carbonic acid component, wherein the chambers communicate with each other for use so that the carbonic acid component solution and the mother liquid are mixed with each other so as to provide a medical solution containing a carbonic acid component, and wherein: the carbonic acid component is contained in the first chamber so that the medical solution after the mixing contains an amount of bicarbonate ions ranging from 10 to 35 mmol/L; and the mother liquid in the second chamber contains an excess of acid, so that after mixing a portion of the carbonic acid component generates carbonic acid (carbonate ions and carbonic acid gas) in the medical solution in an amount ranging from 10 to 80 mmHg.